EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Yang Tang on 05/10/12.

The application has been amended as follows:

Claim 1 has been amended to read as follow:

--"A solid dose controlled release nanoparticulate composition consisting of:

(a) a poorly soluble nanoparticulate drug and at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 50% of the drug particles have an average particle size of less than about 1000 nm when measured by light scattering techniques, and

(b) a rate controlling matrix consists of at least one pharmaceutically acceptable high molecular weight rate-controlling polymer, wherein:

(i) the nanoparticulate drug and the surface stabilizer associated with the surface thereof are dispersed in the high molecular weight rate-controlling polymer throughout the rate controlling matrix,

(ii) the controlled release nanoparticulate composition provides controlled release of the nanoparticulate drug for a time period ranging from about 2 to about 24 hours,

(iii) the concentration of the high molecular weight rate controlling polymer is from about 5 to about 95% (w/w),

(iv) the surface stabilizer is selected from the group consisting of gelatin, lecithin, dextran, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethyl-cellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, tyloxapol, poloxamers, poloxamines, poloxamine 908, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, an alkyl aryl polyether sulfonate, a mixture of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), SA9OHCO, decanoyl-N-methylglucamide, n-decyl -D-glucopyranoside, n-decyl -D-maltopyranoside, n-dodecyl -D-glucopyranoside, n-dodecyl -D-maltoside, heptanoyl-N-methylglucamide, n-heptyl--D-glucopyranoside, n-heptyl -D-thioglucoside, n-hexyl -D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl -D-glucopyranoside,

octanoyl-N-methylglucamide, n-octyl--D-glucopyranoside, and octyl -D-thioglucopyranoside, and

(v) the high molecular weight rate-controlling polymer is selected from the group consisting of polyethylene oxide (PEO), polyvinyl acetate phthalate, gum arabic, agar, guar gum, cereal gums, dextran, casein, gelatin, pectin, carrageenan, waxes, shellac, hydrogenated vegetable oils, polyvinylpyrrolidone, hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcelluose (HPMC), sodium carboxymethylcellulose (CMC), poly(ethylene) oxide, alkyl cellulose, ethyl cellulose, methyl cellulose, carboxymethyl cellulose, hydrophilic cellulose derivatives, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, polyvinyl acetaldiethylamino acetate, poly(alkylmethacrylate), poly(vinyl acetate), polymers derived from acrylic or methacrylic acid and their respective esters, and copolymers derived from acrylic or methacrylic acid and their respective esters."--

Claim 30 has been amended to read as follow:

--"A method of preparing a solid dose controlled release nanoparticulate formulation comprising:

(a) combining a nanoparticulate composition of a nanoparticulate drug, at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 50% of the drug particles have an average particle size of less than

about 1000 nm when measured by light scattering techniques, and at least one pharmaceutically acceptable high molecular weight rate-controlling polymer at a concentration of from about 5% to about 95% (w/w);

(b) forming a solid dose formulation from the mixture of step (a); wherein the high molecular weight rate-controlling polymer forms a rate controlling matrix, and the nanoparticulate drug and the surface stabilizer associated with the surface thereof are dispersed throughout the rate controlling matrix, and

(c) selecting the solid dose formulation which has a controlled release of the nanoparticulate drug following administration for a time period ranging from about 2 to about 24 hours,

wherein the solid dose controlled release nanoparticulate composition consists of:

(1) the nanoparticulate drug and the surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 50% of the drug particles have an average particle size of less than about 1000 nm when measured by light scattering techniques, and

(2) a rate controlling matrix comprised of at least the high molecular weight rate-controlling polymer, wherein:

(i) the nanoparticulate drug and the surface stabilizer associated with the surface thereof are dispersed in the high molecular weight rate-controlling polymer throughout the rate controlling matrix,

(ii) the concentration of the high molecular weight rate controlling polymer is from about 5 to about 95% (w/w),

(iii) the surface stabilizer is selected from the group consisting of gelatin, lecithin, dextran, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethyl-cellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, tyloxapol, poloxamers, poloxamines, poloxamine 908, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, an alkyl aryl polyether sulfonate, a mixture of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), SA9OHCO, decanoyl-N-methylglucamide, n-decyl -D-glucopyranoside, n-decyl -D-maltopyranoside, n-dodecyl -D-glucopyranoside, n-dodecyl -D-maltoside, heptanoyl-N-methylglucamide, n-heptyl--D-glucopyranoside, n-heptyl -D-thioglucoside, n-hexyl -D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl -D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl--D-glucopyranoside, and octyl -D-thioglucopyranoside,

wherein the nanoparticulate drug is in a crystalline phase, an amorphous phase, or a mixture thereof, and

(iv) wherein the high molecular weight rate-controlling polymer is selected from the group consisting of polyethylene oxide (PEO), polyvinyl acetate phthalate, gum arabic, agar, guar gum, cereal gums, dextran, casein, gelatin, pectin, carrageenan, waxes, shellac, hydrogenated vegetable oils, polyvinylpyrrolidone, hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcelluose (HPMC), sodium carboxymethylcellulose (CMC), poly(ethylene) oxide, alkyl cellulose, ethyl cellulose, methyl cellulose, carboxymethyl cellulose, hydrophilic cellulose derivatives, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, polyvinyl acetaldiethylamino acetate, poly(alkylmethacrylate), poly(vinyl acetate), polymers derived from acrylic or methacrylic acid and their respective esters, and copolymers derived from acrylic or methacrylic acid and their respective esters."--

Claim 35 has been amended to read as follow:

--"A method of treating a mammal comprising administering to the mammal an effective amount of a solid dose controlled release nanoparticulate formulation composition, wherein the composition consists of:

(a) the formulation consists of a poorly soluble nanoparticulate drug particles and at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 50% of the drug particles have an average particle size of less than about 1000 nm when measured by light scattering techniques, and

(b) a rate controlling matrix consists of at least one pharmaceutically acceptable high molecular weight rate-controlling polymer, wherein:

(i) at a concentration of from about 5% to about 95% (w/w), wherein the nanoparticulate drug and the surface stabilizer associated with the surface thereof are dispersed in the high molecular weight rate-controlling polymer throughout the rate controlling matrix;

(ii) the formulation has a controlled release of the nanoparticulate drug following administration composition provides controlled release of the nanoparticulate drug for a time period ranging from about 2 to about 24 hours,

(iii) the concentration of the high molecular weight rate controlling polymer is from about 5 to about 95% (w/w),

(iv) wherein the surface stabilizer is selected from the group consisting of gelatin, lecithin, dextran, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethyl-cellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, tyloxapol, poloxamers, poloxamines, poloxamine 908, dialkylesters of sodium sulfosuccinic acid, sodium lauryl

sulfate, an alkyl aryl polyether sulfonate, a mixture of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), SA9OHCO, decanoyl-N-methylglucamide, n-decyl -D-glucopyranoside, n-decyl -D-maltopyranoside, n-dodecyl -D-glucopyranoside, n-dodecyl -D-maltoside, heptanoyl-N-methylglucamide, n-heptyl--D-glucopyranoside, n-heptyl -D-thioglucoside, n-hexyl -D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl -D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl--D-glucopyranoside, and octyl -D-thioglucopyranoside,

wherein the nanoparticulate drug is in a crystalline phase, an amorphous phase, or a mixture thereof, and

(v) wherein the high molecular weight rate-controlling polymer is selected from the group consisting of polyethylene oxide (PEO), polyvinyl acetate phthalate, gum arabic, agar, guar gum, cereal gums, dextran, casein, gelatin, pectin, carrageenan, waxes, shellac, hydrogenated vegetable oils, polyvinylpyrrolidone, hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcelluose (HPMC), sodium carboxymethylcellulose (CMC), poly(ethylene) oxide, alkyl cellulose, ethyl cellulose, methyl cellulose, carboxymethyl cellulose, hydrophilic cellulose derivatives, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, polyvinyl acetaldiethylamino acetate, poly(alkylmethacrylate), poly(vinyl acetate), polymers derived from acrylic or methacrylic acid and their respective esters, and copolymers derived from acrylic or methacrylic acid and their respective esters."--

Claim 14 has been amended to read:

--"A solid dosage form consisting of the controlled release nanoparticulate composition according to claim 1 and at least one auxiliary excipient, wherein the solid dosage form is in a tablet form, a multiparticulate form, or a powder form."--

Claim 16 has been amended to read as follow:

--"The solid dosage form of claim 14, wherein the controlled release nanoparticulate composition and the at least one auxiliary excipient are compressed to form a tablet."--

Claim 18 has been amended to read:

--"The solid dosage form of claim 14, wherein the controlled release nanoparticulate composition and the at least one auxiliary excipient are compressed to form a multilayer tablet."--

Claims 12, 15, 17, 19-22, 25-29, 53 and 54 have been cancelled.

The following is an examiner's statement of reasons for allowance:

The closest prior art, Liversidge et al., does not teach a compressed matrix consisting of high molecular weight rate controlling polymer, a nanoparticulate active agent particle, and a surface modifier adsorbed on the surface of the active agent

particle. Liversidge further does not teach that the nanoparticulate active agent and surface modifier are dispersed in the compressed matrix.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Claims 1, 2, 4, 8, 9, 11, 13, 14, 16, 18, 30, 31, 33-36, 38-40, 42-44, 46-48 and 50-52 are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN TRAN whose telephone number is (571)272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. TRAN/
Primary Examiner, Art Unit 1615